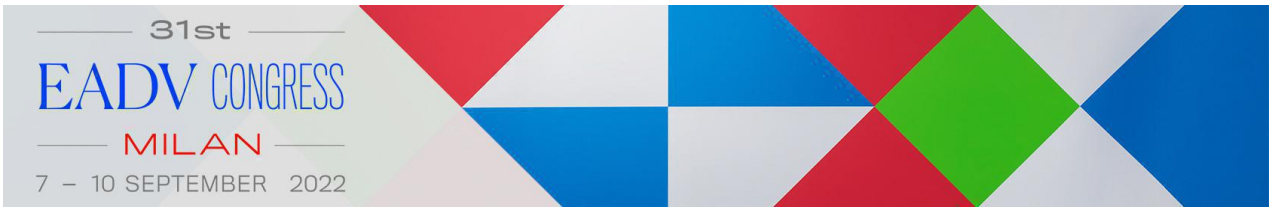

Abstract N°: 3635

Title: Treatment of plaque psoriasis with piclidenoson: Efficacy and safety results from a phase 3 clinical trial (COMFORT)

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Introduction

Overexpression of A3 adenosine receptor (A3AR) has been demonstrated in the skin and peripheral blood mononuclear cells of patients (pts) with psoriasis. Piclidenoson (CF101), an orally bioavailable small molecule A3AR agonist, inhibits IL-17 and IL-23 production in keratinocytes. We present efficacy and safety results from a phase 3 clinical trial (COMFORT, NCT03168256) investigating piclidenoson in moderate-to-severe plaque psoriasis.

Materials and methods

The COMFORT trial was a multicenter, randomized, placebo- and active-controlled, double-blind study in moderate-to-severe plaque psoriasis. Pts were randomized to 4 arms in a 3:3:3:2 ratio (piclidenoson 2 mg BID, piclidenoson 3 mg BID, apremilast 30 mg BID, or placebo). At week 16, pts in the placebo arm were re-randomized (1:1:1) to piclidenoson 2 mg BID, piclidenoson 3 mg BID, or apremilast 30 mg BID. The primary endpoint was Psoriasis Area and Severity Index (PASI) 75 at week 16 vs placebo (superiority). Secondary endpoints included safety and noninferiority of piclidenoson vs apremilast at week 32 in PASI 50 and 75, and Psoriasis Disability Index (PDI). Study duration was 32 weeks with an optional extension to 48 weeks.

Results

A total of 529 pts were randomized and received ≥1 dose of study medication (safety population). The efficacy analyses included 426 pts (piclidenoson 2 mg BID, 127; piclidenoson 3 mg BID 103; apremilast ,118; placebo, 78). Piclidenoson at 2 and 3 mg BID demonstrated equivalent efficacy responses. The study met the primary endpoint with the 3 mg BID dose: at week 16, the rate of PASI 75 response was statistically significantly better in the piclidenoson 3 mg BID arm vs placebo (9.7% vs 2.6%, P=0.037). At week 32, piclidenoson 3 mg was inferior to apremilast with respect to PASI 75 (17.0% vs 26.2%) and PASI 50 (29.1% vs. 44.9%), but superior to apremilast with respect to PDI improvement from baseline (18.4% vs 9.3%, respectively, P<0.05). The PASI responses with piclidenoson continued to increase throughout the study period in a linear manner. At week 48, PASI 50 responses

were 90.0% in the piclidenoson 3 mg BID arm and 100% in the apremilast arm, and PDI improvement from baseline was significantly higher in the piclidenoson 3 mg BID arm than in the apremilast arm (60% vs 10%, P=0.02). The safety profile of piclidenoson was excellent and better than that of apremilast. Gastrointestinal adverse events (AEs) were reported in 6% of the apremilast-treated pts vs 1% of piclidenoson-treated and placebo-treated pts, and the rate of treatment discontinuation was significantly higher in apremilast-treated pts vs piclidenoson-treated pts.

Discussion

Piclidenoson demonstrated an excellent safety profile and efficacy responses that increased in a linear manner over time. The results of this phase 3 study warrant its continued clinical development. A pivotal phase 3 trial is planned.